

## PATENT COOPERATION TREATY

PCT  
**NOTIFICATION OF ELECTION**  
(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
US Department of Commerce  
United States Patent and Trademark  
Office, PCT  
2011 South Clark Place Room  
CP2/5C24  
Arlington, VA 22202  
ETATS-UNIS D'AMERIQUE  
in its capacity as elected Office

Date of mailing (day/month/year) 29 May 2001 (29.05.01)	
International application No. PCT/US00/20981	Applicant's or agent's file reference 29342/36539
International filing date (day/month/year) 01 August 2000 (01.08.00)	Priority date (day/month/year) 03 August 1999 (03.08.99)
<b>Applicant</b> ANDERSON, Neil, R. et al	

1. The designated Office is hereby notified of its election made:

in the demand filed with the International Preliminary Examining Authority on:

06 February 2001 (06.02.01)

in a notice effecting later election filed with the International Bureau on:

\_\_\_\_\_

2. The election  was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer Maria Kirchner  Telephone No.: (41-22) 338.83.38
---	--

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
8 February 2001 (08.02.2001)

PCT

(10) International Publication Number  
**WO 01/08688 A2**

(51) International Patent Classification<sup>7</sup>: A61K 31/4985,  
9/14, A61P 15/10

IN 47906 (US). HARTAUER, Kerry, J. [US/US]; 14907  
Pacer Court, Carmel, IN 46032 (US). KRAL, Martha, A.  
[US/US]; 6125 Haverford Avenue, Indianapolis, IN 46220  
(US). STEPHENSON, Gregory, A. [US/US]; 10227 Bent  
Tree Lane, Fishers, IN 46032 (US).

(21) International Application Number: PCT/US00/20981

(74) Agent: NAPOLI, James, J.; Marshall, O'Toole, Gerstein,  
Murray & Borun, 6300 Sears Tower, 233 S. Wacker Drive,  
Chicago, IL 60606 (US).

(22) International Filing Date: 1 August 2000 (01.08.2000)

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ,  
DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,  
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,  
TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(25) Filing Language: English

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KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian

(26) Publication Language: English

(30) Priority Data:  
60/147,048 3 August 1999 (03.08.1999) US

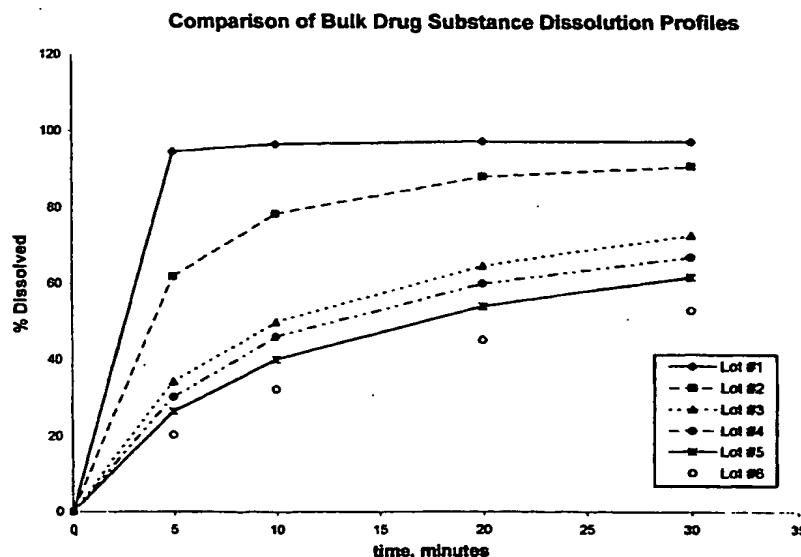
(71) Applicant (*for all designated States except US*): LILLY  
ICOS LLC [US/US]; 1209 Orange Street, Wilmington, DE  
19801 (US).

(72) Inventors; and

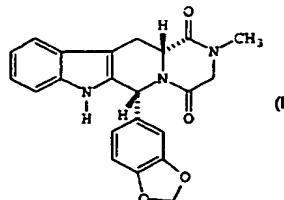
(75) Inventors/Applicants (*for US only*): ANDERSON, Neil,  
R. [US/US]; 906 Northwestern Avenue, West Lafayette,

[Continued on next page]

(54) Title:  $\beta$ -CARBOLINE DRUG PRODUCTS



(57) Abstract: A compound of structural formula (I), and pharmaceutically acceptable salts and solvates thereof, wherein the compound is in free drug particulate form, is disclosed.



WO 01/08688 A2



patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

**Published:**

- *Without international search report and to be republished upon receipt of that report.*

# INTERNATIONAL SEARCH REPORT

Interr. Application No.

PCT/US 00/20981

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 A61K31/4985 A61K9/14 A61P15/10

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
 IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 38131 A (GLAXO GROUP LIMITED) 5 December 1996 (1996-12-05) cited in the application page 5, line 31 -page 6, line 11 page 14, line 13 -page 17, line 4 ---	1-19
A	GB 2 293 103 A (CEPHALON INC.) 20 March 1996 (1996-03-20) page 3, line 1 -page 7, line 15 -----	1-19

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

11 January 2001

Date of mailing of the international search report

09/02/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.  
 Fax: (+31-70) 340-3016

Authorized officer

Benz, K

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/20981

Patent document cited in search report	Publication date	Patent family member(s)			Publication date
WO 9638131	A 05-12-1996	AU 6002696 A			18-12-1996
		EP 0828479 A			18-03-1998
		US 5985326 A			16-11-1999
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GB 2293103	A 20-03-1996	US 5618845 A			08-04-1997
		AT 188607 T			15-01-2000
		AU 3509099 A			19-08-1999
		AU 703087 B			18-03-1999
		AU 3951495 A			02-05-1996
		BG 101389 A			30-12-1997
		BR 9509257 A			07-07-1998
		CA 2201967 A			18-04-1996
		CZ 9701032 A			17-09-1997
		DE 69514497 D			17-02-2000
		DE 69514497 T			10-08-2000
		DK 731698 T			08-05-2000
		EP 0731698 A			18-09-1996
		EP 0966962 A			29-12-1999
		ES 2142499 T			16-04-2000
		FI 971417 A			04-04-1997
		GR 3033152 T			31-08-2000
		HK 1003561 A			30-10-1998
		HU 77778 A			28-08-1998
		JP 2915146 B			05-07-1999
		JP 9511754 T			25-11-1997
		KR 249360 B			01-04-2000
		LT 97060 A, B			27-10-1997
		LV 11852 A			20-10-1997
		LV 11852 B			20-03-1998
		NO 971541 A			04-06-1997
		NZ 295869 A			26-02-1998
		PL 319480 A			04-08-1997
		PT 731698 T			31-05-2000
		SI 9520106 A			28-02-1998
		SK 44597 A			10-09-1997
		WO 9611001 A			18-04-1996
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## PATENT COOPERATION TREATY

PCT

REC'D 27 NOV 2001

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 29342/36539	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/20981	International filing date (day/month/year) 01/08/2000	Priority date (day/month/year) 03/08/1999
International Patent Classification (IPC) or national classification and IPC A61K31/4985		
Applicant LILLY ICOS LLC et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I     Basis of the report
- II     Priority
- III     Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV     Lack of unity of invention
- V     Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI     Certain documents cited
- VII     Certain defects in the international application
- VIII     Certain observations on the international application

Date of submission of the demand 06/02/2001	Date of completion of this report 22.11.2001
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Greif, G  Telephone No. +49 89 2399 8659



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/20981

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):  
**Description, pages:**

1-31                   as originally filed

**Claims, No.:**

1-19                   as originally filed

**Drawings, sheets:**

1/1                   as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description,       pages:
- the claims,              Nos.:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/20981

the drawings, sheets:

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

the entire international application.  
 claims Nos. 7-9 (with respect to IA), 19.

because:

- the said international application, or the said claims Nos. 7-9 (with respect to IA) relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 19, see separate sheet Item III are so unclear that no meaningful opinion could be formed (*specify*):  
**see separate sheet**
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos. .
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- the written form has not been furnished or does not comply with the standard.
- the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N) Yes: Claims 1-18

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/20981

	No:	Claims
Inventive step (IS)	Yes:	Claims 1-18
	No:	Claims
Industrial applicability (IA)	Yes:	Claims 1-6, 10-18
	No:	Claims

2. Citations and explanations  
**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. Claims 7-9 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).
2. Due to lack of functional features, no opinion will be established on the subject-matter of claim 19.

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. The subject-matter of claims 1-18 has not been disclosed in the documents cited in the search report. Claims 1-18 therefore fulfill the requirements of the PCT with respect to novelty and inventive step.
2. For the assessment of the present claims 7-9 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**Re Item VIII**

**Certain observations on the international application**

The term d90=40 or less is not clear and should be replaced by the definition as cited in the description p. 8, line 31 - p. 9, line 2.

**PATENT COOPERATION TREATY**

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

NAPOLI, James, J.  
Marshall, O'Toole, Gerstein, Murray  
6300 Sears Tower  
233 S. Wacker Drive  
Chicago, IL 60606  
ETATS-UNIS D'AMERIQUE

*RECD.*

**PCT**

**NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

(PCT Rule 71.1)

Date of mailing (day/month/year)	22.11.2001
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Applicant's or agent's file reference  
29342/36539

**IMPORTANT NOTIFICATION**

International application No. PCT/US00/20981	International filing date (day/month/year) 01/08/2000	Priority date (day/month/year) 03/08/1999
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Applicant  
LILLY ICOS LLC et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

**4. REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
Fax: +49 89 2399 - 4465

Authorized officer

Senkel, H  
Tel. +49 89 2399-8071



## PATENT COOPERATION TREATY

PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 29342/36539	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/20981	International filing date (day/month/year) 01/08/2000	Priority date (day/month/year) 03/08/1999	
International Patent Classification (IPC) or national classification and IPC A61K31/4985			
Applicant LILLY ICOS LLC et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

- This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I     Basis of the report
- II     Priority
- III     Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV     Lack of unity of invention
- V     Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI     Certain documents cited
- VII     Certain defects in the international application
- VIII     Certain observations on the international application

Date of submission of the demand 06/02/2001	Date of completion of this report 22.11.2001
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Greif, G  Telephone No. +49 89 2399 8659



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/20981

## I. Basis of the report

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):  
**Description, pages:**

1-31                  as originally filed

### Claims, No.:

1-19                  as originally filed

### Drawings, sheets:

1/1                  as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description,        pages:
- the claims,           Nos.:

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/20981

- the drawings,        sheets:
5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):  
*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*
6. Additional observations, if necessary:

### III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- the entire international application.
- claims Nos. 7-9 (with respect to IA), 19.

because:

- the said international application, or the said claims Nos. 7-9 (with respect to IA) relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 19, see separate sheet Item III are so unclear that no meaningful opinion could be formed (*specify*):  
**see separate sheet**
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos. .
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- the written form has not been furnished or does not comply with the standard.
- the computer readable form has not been furnished or does not comply with the standard.

### V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

#### 1. Statement

Novelty (N)                  Yes:      Claims 1-18

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/20981

	No:	Claims
Inventive step (IS)	Yes:	Claims 1-18
	No:	Claims
Industrial applicability (IA)	Yes:	Claims 1-6, 10-18
	No:	Claims

**2. Citations and explanations  
see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/20981

**R Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. Claims 7-9 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).
2. Due to lack of functional features, no opinion will be established on the subject-matter of claim 19.

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. The subject-matter of claims 1-18 has not been disclosed in the documents cited in the search report. Claims 1-18 therefore fulfill the requirements of the PCT with respect to novelty and inventive step.
2. For the assessment of the present claims 7-9 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**Re Item VIII**

**Certain observations on the international application**

The term d90=40 or less is not clear and should be replaced by the definition as cited in the description p. 8, line 31 - p. 9, line 2.

## PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

MARSHALL O'TOOLE GERSTEIN  
 MURRAY & BORUN  
 Attn. NAPOLI, James J.  
 6300 Sears Tower  
 233 South Wacker Drive  
 Chicago, Illinois 60606  
 UNITED STATES OF AMERICA

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT  
OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing  
(day/month/year)

09/02/2001

Applicant's or agent's file reference  
29342/36539

FOR FURTHER ACTION See paragraphs 1 and 4 below

International application No.  
PCT/US 00/ 20981International filing date  
(day/month/year)

01/08/2000

Applicant

LILLY ICOS LLC et al.

DOCKETED: 4/9/01

1.  The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

DOCKETED

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland  
 Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2.  The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3.  With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Further action(s): The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority  
  
 European Patent Office, P.B. 5818 Patentlaan 2  
 NL-2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Jaap Hurenkamp

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the International application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

## NOTES TO FORM PCT/ISA/220 ( continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

**The following examples illustrate the manner in which amendments must be explained in the accompanying letter:**

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

**It must be in the language in which the International application is to be published.**

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for International preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the International application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

**PATENT COOPERATION TREATY**  
**PCT**

**INTERNATIONAL SEARCH REPORT**

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>29342/36539</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 00/20981</b>	International filing date (day/month/year) <b>01/08/2000</b>	(Earliest) Priority Date (day/month/year) <b>03/08/1999</b>
Applicant <b>LILLY ICOS LLC et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

- the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of invention is lacking (see Box II).

4. With regard to the title,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

**BETA-CARBOLINE DRUG PRODUCTS**

5. With regard to the abstract,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

1 \_\_\_\_\_

None of the figures.

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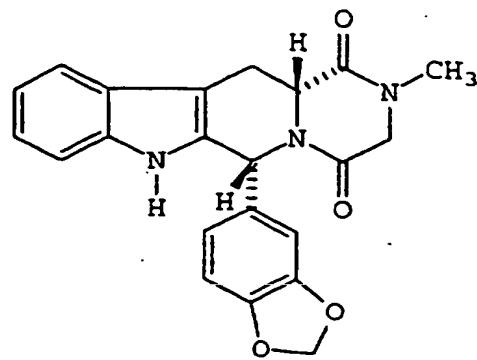
INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 00/20981

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

A compound of structural formula (I), and pharmaceutically acceptable salts and solvates thereof, wherein the compound is in free drug particulate form, is disclosed.



## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/20981

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/4985 A61K9/14 A61P15/10

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 38131 A (GLAXO GROUP LIMITED) 5 December 1996 (1996-12-05) cited in the application page 5, line 31 -page 6, line 11 page 14, line 13 -page 17, line 4 -----	1-19
A	GB 2 293 103 A (CEPHALON INC.) 20 March 1996 (1996-03-20) page 3, line 1 -page 7, line 15 -----	1-19

 Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

## ° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 January 2001	09/02/2001
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer  Benz, K

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/20981

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  

Although claims 7-9 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/20981

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9638131	A 05-12-1996	AU 6002696	A	18-12-1996
		EP 0828479	A	18-03-1998
		US 5985326	A	16-11-1999
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GB 2293103	A 20-03-1996	US 5618845	A	08-04-1997
		AT 188607	T	15-01-2000
		AU 3509099	A	19-08-1999
		AU 703087	B	18-03-1999
		AU 3951495	A	02-05-1996
		BG 101389	A	30-12-1997
		BR 9509257	A	07-07-1998
		CA 2201967	A	18-04-1996
		CZ 9701032	A	17-09-1997
		DE 69514497	D	17-02-2000
		DE 69514497	T	10-08-2000
		DK 731698	T	08-05-2000
		EP 0731698	A	18-09-1996
		EP 0966962	A	29-12-1999
		ES 2142499	T	16-04-2000
		FI 971417	A	04-04-1997
		GR 3033152	T	31-08-2000
		HK 1003561	A	30-10-1998
		HU 77778	A	28-08-1998
		JP 2915146	B	05-07-1999
		JP 9511754	T	25-11-1997
		KR 249360	B	01-04-2000
		LT 97060	A,B	27-10-1997
		LV 11852	A	20-10-1997
		LV 11852	B	20-03-1998
		NO 971541	A	04-06-1997
		NZ 295869	A	26-02-1998
		PL 319480	A	04-08-1997
		PT 731698	T	31-05-2000
		SI 9520106	A	28-02-1998
		SK 44597	A	10-09-1997
		WO 9611001	A	18-04-1996
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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>29342/36539</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 00/20981</b>	International filing date (day/month/year) <b>01/08/2000</b>	(Earliest) Priority Date (day/month/year) <b>03/08/1999</b>
Applicant <b>LILLY ICOS LLC et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
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  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of invention is lacking (see Box II).

4. With regard to the **title**,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

BETA-CARBOLINE DRUG PRODUCTS

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

1

None of the figures.

XSSA29676114 MA

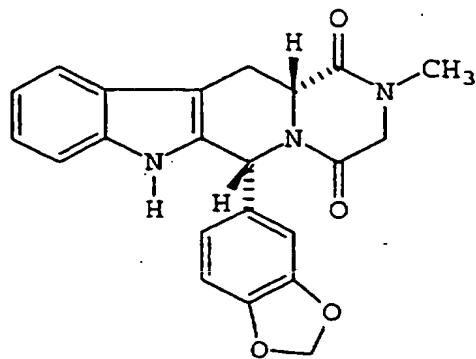
International application No.

INTERNATIONAL SEARCH REPORT

PCT/US 00/20981

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

A compound of structural formula (I), and pharmaceutically acceptable salts and solvates thereof, wherein the compound is in free drug particulate form, is disclosed.



## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/20981

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 A61K31/4985 A61K9/14 A61P15/10

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 38131 A (GLAXO GROUP LIMITED) 5 December 1996 (1996-12-05) cited in the application page 5, line 31 -page 6, line 11 page 14, line 13 -page 17, line 4 ----	1-19
A	GB 2 293 103 A (CEPHALON INC.) 20 March 1996 (1996-03-20) page 3, line 1 -page 7, line 15 -----	1-19



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## ° Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

11 January 2001

Date of mailing of the international search report

09/02/2001

Name and mailing address of the ISA

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 NL 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Benz, K

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/20981

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9638131	A	05-12-1996	AU	6002696 A	18-12-1996
			EP	0828479 A	18-03-1998
			US	5985326 A	16-11-1999
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GB 2293103	A	20-03-1996	US	5618845 A	08-04-1997
			AT	188607 T	15-01-2000
			AU	3509099 A	19-08-1999
			AU	703087 B	18-03-1999
			AU	3951495 A	02-05-1996
			BG	101389 A	30-12-1997
			BR	9509257 A	07-07-1998
			CA	2201967 A	18-04-1996
			CZ	9701032 A	17-09-1997
			DE	69514497 D	17-02-2000
			DE	69514497 T	10-08-2000
			DK	731698 T	08-05-2000
			EP	0731698 A	18-09-1996
			EP	0966962 A	29-12-1999
			ES	2142499 T	16-04-2000
			FI	971417 A	04-04-1997
			GR	3033152 T	31-08-2000
			HK	1003561 A	30-10-1998
			HU	77778 A	28-08-1998
			JP	2915146 B	05-07-1999
			JP	9511754 T	25-11-1997
			KR	249360 B	01-04-2000
			LT	97060 A, B	27-10-1997
			LV	11852 A	20-10-1997
			LV	11852 B	20-03-1998
			NO	971541 A	04-06-1997
			NZ	295869 A	26-02-1998
			PL	319480 A	04-08-1997
			PT	731698 T	31-05-2000
			SI	9520106 A	28-02-1998
			SK	44597 A	10-09-1997
			WO	9611001 A	18-04-1996
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